PATENT COOPERATION TREATY

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From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

Amersham Biosciences AB
Patents Department
Björkgatan 30
SE-751 84 Uppsala
Sweden

11 Apr 2006
RD
AK ✓
14/2/06
PU0407-PCT

PCT U-A PD

WRITTEN OPINION OF THE INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

(PCT Rule 66)

Date of mailing *(day/month/year)*	10 -02- 2006
Applicant's or agent's file reference: PU0407-PCT	REPLY DUE: within 60 days from the above date of mailing

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/SE2005/000229 ✓	21.02.2005 ✓	26.02.2004

International Patent Classification (IPC) or both national classification and IPC
See Supplemental Box

Applicant
AMERSHAM BIOSCIENCES AB et al

1. ☒ The written opinion established by the International Searching Authority:
   ☒ is ☐ is not
   considered to be a written opinion of the International Preliminary Examining Authority.

2. This second (first, etc.) opinion contains indications relating to the following items:
   - ☒ Box No. I Basis of the opinion
   - ☐ Box No. II Priority
   - ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - ☐ Box No. IV Lack of unity of invention
   - ☒ Box No. V Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - ☐ Box No. VI Certain documents cited
   - ☐ Box No. VII Certain defects in the international application
   - ☒ Box No. VIII Certain observations on the international application

3. The applicant is hereby invited to reply to this opinion.
   When? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(e).
   How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.
   Also For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4*bis*. For an informal communication with the examiner, see Rule 66.6. For an additional opportunity to submit amendments, see Rule 66.4.

   If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary report on patentability (Chapter II of the PCT) must be established according to Rule 69.2 is: 26.06.2006

Name and mailing address of the IPEA/SE
Patent- och registreringsverket
Box 5055
S-102 42 STOCKHOLM
Facsimile No. 46 8 667 72 88

Authorized officer
Moa Grönkvist/MP
Telephone No. 46 8 782 25 00

International application No.
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Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of: Cover sheet

INTERNATIONAL PATENT CLASSIFICATION (IPC):

C12N 15/10 (2006.01)
B01D 15/08 (2006.01)

WRITTEN OPINION OF THE INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

International application No.
PCT/SE2005/000229

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of:

☒ the international application in the language in which it was filed

☐ a translation of the international application into _____ ,
which is the language of a translation furnished for the purposes of:

- ☐ international search (Rules 12.3(a) and 23.1(b))
- ☐ publication of the international application (Rule 12.4(a))
- ☐ international preliminary examination (Rules 55.2(a) and/or 55.3(a))

2. With regard to the elements of the international application, this opinion has been established on the basis of *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed."):*

☐ the international application as originally filed/furnished

☐ the description:

pages _____ as originally filed/furnished
pages _____ received by this Authority on _____
pages _____ received by this Authority on _____

☐ the claims:

pages _____ as originally filed/furnished
pages _____ as amended (together with any statement) under Article 19
pages _____ received by this Authority on _____
pages _____ received by this Authority on _____

☐ the drawings:

pages _____ as originally filed/furnished
pages _____ received by this Authority on _____
pages _____ received by this Authority on _____

☐ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages _____
- ☐ the claims, Nos. _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing *(specify)*: _____
- ☐ any table(s) related to the sequence listing *(specify)*: _____

4. ☐ This opinion has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

- ☐ the description, pages _____
- ☐ the claims, Nos. _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing *(specify)*: _____
- ☐ any table(s) related to the sequence listing *(specify)*: _____

WRITTEN OPINION OF THE INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

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Box No. V **Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	1,2,11,12
	Claims	
Inventive step (IS)	Claims	1-6,9-15,17-22
	Claims	
Industrial applicability (IA)	Claims	
	Claims	

2. Citations and explanations:

The invention relates to methods for the isolation of plasmids using a separation matrix with anion exchange groups. The chosen pore size distribution does not allow access of plasmids to the pore surfaces.

The most relevant documents cited in the International Search Report are:

D1: WO9963076A1
D2: WO0137987A1
D3: US6270970B1

Document D1 discloses a method of purifying plasmids using a TMAE anion exchange chromatographic column (see claims 1-3). The used matrix is a fractogel TMAE anion exchange resin. These resins are known to have particle sizes between 20-40 µm for TMAE S and 40-90 µm for TMAE M. The pore size is about 800 Å (see Merck website).

Thus, D1 is considered to disclose a method of isolating plasmids with the steps of

(a) providing a separation matrix comprised of porous carriers, which carrier present anion exchange groups on external surfaces as well as pore surfaces and a pore size distribution that does not allow access of plasmids to pore surfaces;
(b) contacting said matrix with a liquid to absorb plasmids to ligands present on the external surfaces of the separation matrix

.../...

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of: V

Document D2 discloses separation methods for plasmids. In example 3 a separation of plasmids is performed with anion exchange chromatography. The plasmids are bound to the separation medium B and its charged outer surfaces of the anion-exchanger. It is not stated that the plasmids have access to the pores.

Document D3 relates to mixed-bed solid phases for isolation of nucleic acids such as plasmids. The solid phase of the different beds comprise magnetic silica particles (particle size below 15 µm), see column 12. The solid phase can be with or without pores with size sufficiently large to admit the target nucleic acid in to the interior of the particles. The anion exchanger phase can be Sepharose but is not limited thereto.

With background of D1-D3, and as a consequence of unclear claims (see box VIII), the method according to claim 1 and the use according to claim 11 lacks novelty. Further, the DNA exclusion limits covered by D1-D3 are assumed to be at least about 270 base pairs. Therefore, also claims 2 and 12 lacks novelty.

The claims 3-6, 9-10, 13-15 and 17 are considered to involve particular detail executions obvious to a person skilled in the art. Therefore, the invention according to these claims is not considered to involve an inventive step.

It is also considered to be obvious to a person skilled in the art to develop a kit for the method described in D1 or D2. Therefore the invention according to claims 18-22 lacks an inventive step.

WRITTEN OPINION OF THE
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

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Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claims 1, 11 and 18 do not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not clearly defined. The claims attempts to define the subject-matter in terms of the result to be achieved (...pore size distribution that does not allow access of plasmids...) which merely amounts to a statement of the underlying problem. The technical features necessary for achieving this result should be added.

In claims 2, 12 and 19 the matrix is characterised by a DNA exclusion limit of at least about 270 base pairs. This way of characterising a matrix is known in the field but is not a common way of defining and comparing gels. Further, the limit of "about" 270 base pairs is unclear (see PCT GL 5.38).

Claims 1-2, 11-12 and 18-19 have been drafted as separate independent claims of the same category. They appear to relate effectively to the same subject-matter and to differ from each other only with regard to the choice of specific words. The aforementioned claims therefore lack conciseness. See PCT Article 6 and 5.42 Guidelines.